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Demographic and dietary predictors of urinary bisphenol A concentrations in adults in Israel

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ABSTRACT

Background: To date, there is scarce data on levels of exposure to bisphenol A (BPA) in the general population in Israel and the region. The goal of the current study was to measure urinary levels of BPA in the general adult population in Israel and to determine the demographic and dietary predictors of exposure.
Methods: We recruited 249 individuals (ages 20–74) from five different regions in Israel. We collected urine samples and questionnaire data including detailed dietary data and analyzed urine samples for BPA concentrations.
Results: Eighty nine percent of the study population had urinary BPA concentrations equal to or above the level of quantification (0.3 μg/L). Median creatinine adjusted BPA urinary concentrations in the study population (2.3 μg/g) were slightly higher than those reported for the general population in the US (1.76 μg/g) and Canada (1.47 μg/g), and were comparable to those reported for the general population in Belgium (2.25 μg/g) and Korea (2.09 μg/g). BPA concentrations were higher in Jews compared to Arab and Druze (prevalence ratio (PR) = 2.34; 95%CI 1.56–3.49), in individuals with higher education (PR = 1.70, 1.11–2.62), in individuals consuming mushrooms (PR = 2.08, 1.07–4.05), and in smokers (PR = 1.43, 1.00–2.05).
Conclusions: We found that the general adult population in Israel is widely exposed to BPA. Our findings on higher BPA levels in Jews compared to Arabs and Druze and in individuals with higher education highlights the fact that predictors of BPA exposure vary across populations.
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Introduction

Bisphenol A (BPA) is a monomer used in the production of polycarbonate plastics and resins that can be used in food container linings, medical equipment, paper, and cigarette filters (Chapin et al., 2008). Due to BPA's ability to leach from food and beverage containers, and because of its widespread occurrence in the environment, many populations worldwide have nearly ubiquitous exposure to BPA (Vandenberg et al., 2010). The National Toxicology Program has expressed "some concern" that current human exposure to BPA can result in adverse effects on brain development and behavior in fetuses, infants, and children (Chapin et al., 2008). Human studies on the health effects of BPA are limited, although studies have indicated associations between BPA exposure and adverse perinatal, childhood, and adult health outcomes, including reproductive and developmental effects, metabolic disease, and other health effects (Rochester, 2013).

Previous studies have examined the association between individual exposure to BPA and specific products and activities (canned foods, polycarbonate bottles, smoking and alcohol consumption, medical procedures and dental sealants) and demographic variables (age, gender, household income) (Lakind and Naiman, 2011). In many cases, the findings of such studies have been inconsistent. For example, while several studies have found that canned fish and exposure to smoke or second hand smoke are important sources of exposure to BPA in the general population (Braun et al., 2011; Casas et al., 2013), others studies have reported no such association (Lakind and Naiman, 2011). Therefore, there is a need for further study on sources and pathways of BPA exposure, and on predictors of exposure, in various worldwide populations. The goal of the

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current study was to measure urinary levels of BPA in the general adult population in Israel and to determine the demographic and dietary predictors of exposure.

Materials and methods

Study participants

Participants were Israeli adults recruited to the Israel Ministry of Health Biomonitoring Study, a cross-sectional study on exposure of Israeli adults from the general population to environmental chemicals and phytoestrogens (Berman et al., 2013a,b). Israeli adults aged 20–74 were recruited and interviewed between February and June 2011.

The parameters for defining the sample were selected so as to represent the population distribution of urban vs rural dwelling and the two major ethnic groups in Israel (Jews and Arabs), as well as wide geographical representation. Overall, 20 residential areas were selected, with 4 representing the Arab sector (3 urban, 1 rural) and the others the Jewish sector (15 urban, 1 rural). In each residential area, interviewers were requested to interview 15 people. Within each residential area, interviewers were required to select 5 separate areas. Within each area, recruitment was done by "knocking on doors" and interviewing those who met the inclusion criteria and agreed to participate, including providing a urine sample. For each address visited, where there were individuals who refused to participate in the study or were not at home, this was documented. The response rate was 29%, excluding individuals not eligible for the study and individuals not home at the time of the visit. Participants were not targeted for specific exposure scenarios and were not included or excluded on the basis of their potential for low or high exposures to environmental chemicals.

The study protocol was reviewed and approved by the Sheba Tel Hashomer Helsinki Committee. Written informed consent was obtained for all respondents. Participation in the study was voluntary. At the time of recruitment participants received a letter explaining that they would receive individual results on urinary concentrations of environmental contaminants if they requested it at the time of their interview or if their individual urinary metabolite results were unusual. All analysis of data for the study was conducted without details on the identity of the participants.

Out of 249 individuals recruited to the biomonitoring study we measured urinary BPA concentrations for 247. In two individuals the urine volume was insufficient for the analysis. One individual with very high BPA urinary concentrations was excluded from the analysis of demographic and dietary predictors.

Questionnaire and data collection

A trained interviewer administered a detailed structured questionnaire to study participants. The interviews were carried out in Hebrew or Arabic. The interview included a 24 h dietary recall, an adapted food frequency questionnaire, a demographic questionnaire and a health/lifestyle questionnaire. The questionnaire included specific questions on occupation, on consumption of water from water coolers and sports bottles, and on frequency of heating food in the microwave. Socio-demographic and personal variables included age (analyzed as a continuous variable, and in addition grouped as 20–44 years and 45–74 years), gender (males/females), urbanicity (urban/rural), country of birth (Israel/other), education (school level qualification or below [hereafter, lower education/higher education]), household income, and ethnicity (Jewish/Arab and Druze).

Smoking status was based on self-report. Questions used for active tobacco smoking status were: "Do you currently smoke, including a hookah (water pipe)?", "What do you currently smoke, or what did you smoke before? (cigarettes, cigars, pipe, hookah, other), "How many cigarettes do you smoke per day or per week?" Based on the first question, participants were grouped as tobacco smokers (of any kind) or nonsmokers.

Urine sample collection

Spot urine samples were collected in 120-mL urine specimen containers at the time of interview. Urine containers were pretested to ensure that they did not contain BPA. All urine samples were maintained at 4 °C for a maximum of 24 h until they were transported to Sheba Medical Center (SMC) at Tel Hashomer. Urine samples were aliquoted at SMC and frozen at −20 °C. Within four months of collection, urine samples were shipped to the University of Erlangen-Nuremberg in Germany on dry ice (−70 °C), where they were analyzed.

Sample analysis

The determination of bisphenol A was carried out using a gas chromatographic–tandem mass spectrometric (GC–MS/MS) method (Schmidt et al., 2013). The method comprised an enzymatic cleavage of the conjugated phenolic substance, a solid phase extraction of the analyte and a derivatization with N-tert-butyldimethylsilyl-N-methyltrifluoroacetamide (MTBSTFA). An isotope-labeled equivalent was used as an internal standard. Calibration was performed using standard solutions in pooled human urine. Limit of detection (LOD) was 0.1 μg/L and limit of quantification (LOQ) was 0.3 μg/L.

Cotinine in urine was determined using a gas chromatography mass spectrometry procedure proofed and published by the working group "Analyses in biological materials" (Müller, 2003). In brief, cotinine was extracted from the urine using dichloromethane and quantified after gas chromatographic separation by mass spectrometry in single ion monitoring mode (Eckert et al., 2011). Deuterated cotinine was used as an internal standard. Calibration was performed using calibration standards which were prepared in pooled non-smoker urine and which were treated in the same manner as the samples to be analyzed. LOD was 0.5 μg/L and LOQ was 1 μg/L. Creatinine in urine was determined according to the Jaffé method (Larsen, 1972).

Statistical analysis

We used STATA v. 12.1 and SAS 8.2 for descriptive and inference statistics. We calculated geometric means, 95th percentile confidence intervals, percentiles (50th, 75th, 90th) and their confidence intervals for urinary analyte concentrations and for creatinine-adjusted analytes. Concentrations below the limit of quantification (LOQ) for an analyte were replaced by the limit of detection (LOD) for that analyte, and concentrations below the LOD were replaced with the LOD divided by the square root of 2 according to the statistical model by Hornung and Reed (1990).

In a univariate analysis we compared geometric means of urinary BPA between demographic and dietary subgroups using a ratio *t*-test procedure on a lognormal distribution, using both unadjusted and creatinine-adjusted values. Differences between subgroups were also assessed based on ratios obtained from univariate linear regression, with subgroup indicator as an independent factor and log-transformed BPA as a dependent variable. As part of a sensitivity analysis, we adjusted the effect of factors found significantly associated with creatinine-adjusted BPA levels by gender, assuming a residual impact of gender on BPA, even after adjustment to creatinine.

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